UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/063,599	05/03/2002	Dan L. Eaton	10466/365	4659

9157 7590 06/24/2004

GENENTECH, INC.
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080

EXAMINER	
WEGERT, SANDRA L	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 06/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/063,599	EATON ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 9/13/02.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-6 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-6 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 13 May 2002 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9/13/02.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, and/or Claims

The Preliminary Amendment, submitted 9 September 2002, and the Information Disclosure Statement, submitted 13 September 2002, have been entered. Claims 1-6 have been entered.

Claims 1-6 are under examination in the Instant Application.

Informalities

Specification

The disclosure is objected to because of the following informalities:

URL's

The disclosure is objected to because it contains browser-executable code. This occurs, for example, in paragraphs 206. All URL's should be removed from the Specification. Applicant may refer to web sites by non-executable name only. See MPEP § 608.01 (p).

Appropriate correction is required.

Claim Rejections/Objections

Claim Rejections - 35 USC § 101 and 35 USC § 112, first paragraph

The following is a quotation of 35 U.S.C. 101:

> **Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof may obtain a patent therefor, subject to the conditions and requirements of this title.**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention lacks a credible, specific and substantial asserted utility or a well-established utility.

The claims are directed to antibodies made against the polypeptide of SEQ ID NO: 92 (see Specification: Figure 92, *PRO1327* or *DNA66521-1583*). Further limiting claims are presented to monoclonal antibodies, humanized antibodies, antibody fragments, labeled antibodies, and antibodies that bind "specifically" to the polypeptide. However, the specification does not disclose a function for the antibodies against SEQ ID NO: 92, in the context of the cell or organism.

The instant Specification indicates that the protein of SEQ ID NO: 92 is a secreted protein with a variety of functions:

" Secreted proteins have various industrial applications, including as pharmaceuticals, diagnostics, biosensors and bioreactors. Most protein drugs available at present, such as thrombolytic agents, interferons, interleukins, erythropoietins, colony stimulating factors, and various other cytokines, are secretory proteins. Their receptors, which are membrane proteins, also have potential as therapeutic or diagnostic agents. Efforts are being undertaken by both industry and academia to identify new, native secreted proteins. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel secreted proteins." (Paragraph 4).

No well-established utility exists for newly isolated complex biological molecules. However, the specification implies that the following are credible, specific and substantial patentable utilities for the claimed antibodies:

1) In assays to screen for compounds capable of modifying the interaction between receptor and ligand.

2) To bind the polypeptide of SEQ ID NO: 92.

3) To develop drugs for the treatment or prevention of polypeptide deficiency.

4) To treat cancer.

Each of these shall be addressed in turn.

1) in assays to screen for compounds capable of modifying the interaction between receptor and ligand. This asserted utility is credible and substantial but not specific. Such can be performed for any receptor-ligand pair. Additionally, the specification discloses nothing specific or substantial for the compounds that can be identified by this method.

2) To bind the polypeptide of SEQ ID NO: 92. This asserted utility is credible and substantial, but not specific. Antibodies can be made to any polypeptide. However, if the specification discloses nothing specific and substantial about the polypeptide, both the polypeptide and its antibodies have no patentable utility.

3) to develop drugs for the treatment or prevention of polypeptide deficiency. This asserted utility is credible and specific, however, it is not substantial. The specification does not disclose any conditions wherein there is a deficiency of the polypeptides encoded by the claimed polynucleotides. Significant further experimentation would be required of the skilled artisan to identify individuals who would benefit from such a drug, and then to determine a best course of treatment. There is no disclosure, for example, of dosages, nor how to assay for improvement or

intolerable levels of side effects, etc. Since this asserted utility is not presented in mature form, so that it could be readily used in a real world sense, the asserted utility is not substantial.

4) To treat cancer. The Specification implies that antagonists (e.g., antibodies) directed against the protein encoded by DNA66521-1583 (PRO1327) would be expected to have utility in cancer therapy.

Paragraph 512 appears to list the results of tissue expression experiments:

"upregulation of Molecule expression in: as compared to: DNA66521-1583 normal esophagus esophageal tumor normal stomach stomach tumor normal lung lung tumor normal rectum rectum tumor normal skin melanoma tumor "

However, the specification discloses several tissues that express the PRO1327 polypeptide without listing the level of expression or the expression relative to control tissues. Furthermore the Applicant implies that this expression pattern supports a function for the PRO1327 polypeptide in the treatment of cancer. However, evidence of mere expression in a tissue is not tantamount to a showing of a role for the disclosed polynucleotide encoding the claimed polypeptide. It is not clear if expression of the PRO1327 polypeptide is correlated with a specific change in physiology, for example, or with a disease such as cancer.

Furthermore, although the specification teaches that PRO1327 may be expressed more highly in normal lung, and normal skin, the state of the art is such that protein expression levels cannot be accurately predicted from the level of corresponding mRNA transcript, and therefore cannot be correlated to antibody binding. Haynes et al, for example, studied 80 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between protein and transcript levels (Haynes et al., 1998, Electrophoresis 19:1862-1872). That

research group found that for some genes, equivalent mRNA levels translated into protein abundances which varied by more than 50-fold (pg 1863, paragraph 2, Figure 1). Therefore, one skilled in the art cannot predict that the PRO1327 mRNA transcript levels measured in two cancerous tissues are indicative of PRO1327 polypeptide expression in cancerous cells. Undue experimentation is required by the skilled artisan to detect and quantify PRO1327 polypeptide expression in all possible tumor tissues/cells, other than lung, colon or melanoma cancer.

Claims 1-6 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Thus, because the polypeptide of SEQ ID NO: 92 has not been shown to be useful, antibodies made against the polypeptide also have no specific use. Applicants have implied that the PRO1327 polypeptide is a secreted protein, which possesses amino acid sequence identity with neurexophilin family. Regardless of whether the polypeptide of SEQ ID NO: 92 comprises domains from the neurexophilin family of proteins, no specific function has been assigned to the polypeptide. Therefore an antibody that specifically binds the protein of SEQ ID NO 349 would also have no specific function.

Generally, the art acknowledges that function cannot be predicted based solely on structural similarity to a protein found in the sequence databases. For example, Skolnick et al. (2000, Trends in Biotech. 18:34-39) state that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Similarly, Bork (2000, Genome Research

10:398-400) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database (see especially p. 399). Such concerns are also echoed by Doerks et al. (1998, Trends in Genetics 14:248-250) who state that (1) functional information is only partially annotated in the database, ignoring multi functionality, resulting in underpredictions of functionality of a new protein and (2) overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Examples from the secreted polypeptide art demonstrate, in some cases, polypeptides with high homology having a wide-variety of functions in organisms (see Hesselgesser, et al, 1997, Methods in Enzymology, 287: 59-69, see pages 59 and 64-66) and in other cases, many different possible structures for secreted proteins that are considered related as to function (Blease, et al, 2000, Resp. Res., 1(1): 54-61). However, Applicants have not associated the disclosed PRO1327 polypeptide with any type or genus of polypeptide.

Based on the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan how to use the claimed antibodies against PRO1327 without resorting to undue experimentation to determine what the specific biological activities of the PRO1327 polypeptide are.

The specification does not teach the skilled artisan how to use the claimed antibodies directed to the polypeptide of SEQ ID NO: 92 for any purpose. For example, there is no disclosure of particular disease states correlating to an alteration in levels or forms of the

polypeptide such that the claimed antibody could be used as a diagnostic tool. The skilled artisan is not provided with sufficient guidance to use the claimed antibodies for any purpose.

Due to the large quantity of experimentation necessary to determine an activity or property of the disclosed polypeptide such that it can be determined how to use the claimed antibodies directed against SEQ ID NO: 92 and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity to other similar polypeptides, the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite particular biological activities- undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

Claims 1 and 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites an antibody that binds a protein. Claim 6 recites an antibody that "specifically binds to" the same protein. Neither the Specification nor the art provides unambiguous definitions for "binds" and "specifically binds;" therefore, the metes and bounds of

the claims cannot be determined by one skilled in the art. Furthermore, since antibodies are generally seen as binding antigens with both high affinity *and* high specificity, it is not known what additional characteristics would be displayed by an antibody binding "specifically."

Conclusion: Claims 1-6 are rejected for the reasons recited above.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (571) 272-0887.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

SLW
6/15/04

ELIZABETH KEMMERER
PRIMARY EXAMINER